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EXAMINER

GUNTER, DAVID R

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/903,290

Applicant(s)

SINGH ET AL.

Examiner

David R. Gunter

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 6 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Status of the Application

1. The examiner acknowledges the applicant's claim to priority for the current application based on U.S. Provisional Application No. 60/217,624 filed July 11, 2000. Claims 1-4 of the application are pending.

Specification

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. Regarding Claim 1, lines 3-5, the phrase "said primer comprises a first sequence that hybridizes to a first portion of said target sequence and a member of said effector system" is unclear. It is not clear whether the primer comprises both a first sequence and a member of the effector system, or whether the primer comprises a first sequence that hybridizes to both a first portion of the target sequence and a member of the effector system. For the purpose of examination, the Claim will be interpreted to mean that the primer comprises two elements, a sequence which hybridizes and a member of an effector system. However, the claim should be amended to clarify the association between the primer and the effector.
- b. Regarding Claim 1, line 5, the term "effector system" is unclear because it is not clearly defined in the claims or specification. The effector system is defined only in terms of its function, which leaves the nature of the system indefinite. The claims should be amended to define the components of the effector system.
- c. Regarding Claim 1, line 13, the term "substantially stably" in the phrase "where said primer substantially stably binds to said first sequence" is a relative term which renders the claim indefinite. The term "substantially stably" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "substantially stably" may be either deleted so that the claim reads "where said primer binds to said first sequence" or the term must be defined in such a way that the nature and stability of the binding of the primer to the target sequence is clear.

d. Regarding Claim 1, line 13, the term "reversibly binds" in the phrase "said probe reversibly binds to said second sequence" is unclear. Any hybridization of two nucleic acid sequences can be reversed by a sufficient increase in temperature. In addition, specifying that the binding of the probe is reversible implies that the binding of the primer is not reversible. The term "reversibly" may be either deleted so that the claim read "said probe binds to said second sequence" or the term must be defined in such a way that the nature of the binding of the probe to the target sequence is clear.

d. Regarding Claim 2, the phrase "when said labile linkage is hybridized to said member" lacks antecedent basis. Claim 1 does not recite that the labile linkage hybridizes to any component of the effector system, nor does it recite that the members of the effector system hybridize to any of the other molecules recited in the method.

4. The term "any additional members of said effector system" in line 10 of Claim 1 is a relative term which renders the claim indefinite. The claim does not define the additional members of the effector system, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claims do not recite any criteria for determining the identity of the additional members of the effector system, and so the scope of the claim is indefinite. The claim should be amended to identify the members of the effector system.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogan, et al., U.S. Patent Number 5,451,503, filed June 7, 1994, issued September 19, 1995 (hereinafter referred to as "Hogan") in light of Dreyer and Dervan, Proceedings of the National Academy of Sciences of the United States of America. 82:968-972, 1985 (hereinafter referred to as "Dreyer"). The Claims of the instant application recite a method for detection of a target nucleic acid sequence in which two oligonucleotides (designated as the "primer" and the "probe"). The first sequence of the primer hybridizes to a first portion of the target sequence and a member of an effector system. The probe comprises a second sequence that hybridizes to a second portion of the target sequence and a tag specific to the target sequence linked to the second sequence through a labile linkage. The target nucleic acid, probe, primer, and additional members of the effector system are combined under conditions that allow hybridization of the probe and primer to the target sequence and subsequent cleavage of the labile linkage, releasing the tag from the probe. Analysis of the released tags allows detection of the target nucleic acid sequence.

Hogan discloses "novel nucleic acid probes ... which can form a detectable structure only in the presence of a target nucleic acid" (Column 1, lines 38-40) that "can be used to detect nucleic acids" (Column 1, lines 46-47). Hogan discloses two oligonucleotides, each of which has a first and second sequence. The first sequence of the first oligonucleotide binds to a specific

portion of the target, and the first sequence of the second oligonucleotide binds to a second specific portion of the target. The second sequences of the oligonucleotides are complementary to one another, and so hybridize to form a double stranded region (Column 1, 53-67; also Figure 1A). Hogan discloses numerous methods of detecting the formation of the double stranded region including adding "a restriction endonuclease and detecting the cleavage of the ... nucleic acid molecules" (Column 2, lines 33-36).

a. Regarding Claim 1, Hogan discloses the embodiment in which two oligonucleotides (equivalent to the "primer" and "probe" of the instant application) each comprise a region which hybridizes to a target nucleic acid (Column 1, 53-67; also Figure 1A). The instant application (Page 4, lines 14-16) discloses that "the effector moiety ... may provide a complex that results in providing a labile linkage in the probe." After binding the target nucleic acid sequence, the first oligonucleotide of the method of Hogan (equivalent to the "primer" of the instant application) binds to the second oligonucleotide (equivalent to the "probe" of the instant application) to form a double stranded nucleic acid molecule comprising a specific sequence that is recognized by a restriction endonuclease (Column 2, lines 33-36). This formation of an endonuclease binding site satisfies the definition of "providing a labile linkage" given by the specification.

Hogan further discloses the embodiments in which the double stranded polynucleotide formed by the first and second primers are cleaved and the cleaved portion of the polynucleotide is detected (Column 2, line 33-36). In this embodiment, the cleaved portion of the polynucleotide acts as a tag which may be detected, and the detection of which indicates the presence of the target nucleic acid.

b. Regarding Claim 2, Hogan discloses the embodiment in which the oligonucleotides (equivalent to the "primer" and "probe" of the instant application) "can be DNA, modified DNA, RNA, modified RNA, or various combinations thereof" (Column 6, lines 13-15).

c. Regarding Claim 3, Hogan discloses the embodiment in which the labile linkage is "susceptible to double-strand specific chemical cleavage (e.g. using an Iron-EDTA complex)" (Column 4, lines 32-35). Hogan does not specifically teach the use of an electron receptor to reduce the metalloorganic moiety, but the requirement for such a reducing agent is well known in the art and is inherent to method disclosed by Hogan. For example, Dreyer teaches that "the efficiency of the DNA cleavage reaction is dependent on the addition of both the Fe(II) and reducing agent (dithithreitol)" (Abstract, lines 18-20).

d. Regarding Claim 4, Hogan discloses the embodiment in which the oligonucleotides (equivalent to the "primer" and "probe" of the instant application) are cleaved by a restriction enzyme (Column 2, line 33-36).

Conclusion

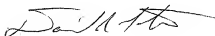
6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701. The examiner can normally be reached on 9:00 - 5:00 M - F.


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.



David R. Gunter, DVM, PhD
August 23, 2002


STEPHANIE W. ZITOMER
PRIMARY EXAMINER